Pessimistic prophets

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Although *nuclear imaging is synonymous with molecular imaging and thus in practice for the last 5 decades,* both Drs. Sadeghi and Carrio, the pro and con authors about whether Molecular Nuclear Cardiology is ready for Prime Time, have come to the same conclusion—that *the cupboard is bare; there is 'no there there.'* Beyond the perfusion imaging, there is no new, clinically compelling, application of radionuclide imaging applications for clinical decision making in nuclear cardiology. There are instances, such as identification of sites of infection of an implanted cardiac device with FDG PET/CT[1,2] that are clinically useful, but have not been widely approved for reimbursement. Similarly, I-123 MIBG myocardial imaging in patients with heart failure demonstrated its prognostic utility in a multinational clinical trial, but has not been widely adopted for clinical decision making.[3,4] There are many other agents in early clinical trials, such as NaF imaging to identify nascent calcification in atheroma, which will require robust data to develop the compelling case for regulatory approval.[5,6]

Rest/stress myocardial perfusion imaging, described almost five decades ago,[7] when criteria for reimbursement were different, addressed a major clinical problem—selection of patients for invasive coronary angiography to identify those in need of revascularization. Clinicians have embraced this noninvasive strategy as a valuable tool to assist clinical care.[8] During these five decades, the population has become more aware of the importance of risk factors, and the medicine and technology have evolved. As a result, the incidence of death from cardiovascular disease has decreased,[9] the incidence of ischemia on myocardial perfusion scans has decreased,[10] and the frequency of performing myocardial perfusion scans has decreased[11] with the introduction of appropriate use criteria,[12] and widespread use of competing technologies including 3-D transthoracic echocardiography,[13] delayed contrast enhancement upon magnetic resonance imaging to detect areas of myocardial necrosis,[14,15] CT coronary angiography for plaque characterization,[16] and fractional (FFR) or coronary flow reserve (CFR).[17]

At this moment, it is unlikely that there will be another single 'killer app' for molecular nuclear cardiology. It is more likely that procedures in combination with anatomical imaging procedures (such as CT or MR imaging) will be developed. For example, molecular imaging with available agents such as rubidium-82 and nitrogen-13 ammonia have been validated for the measurement of CFR.[18] This kinetic analysis technique offers objective criteria to determine if a region of decreased tracer uptake on a perfusion scan is an anatomic variant or a significant lesion. The combined advantages of high resolution and absolute quantitation with PET/CT enhance the clinical utility of perfusion imaging. The combination of PET/MRI would allow an opportunity to simultaneously measure myocyte perfusion, mitochondrial potential, and amino acid incorporation.[19,20] PET/MRI techniques will evolve gradually and are expected to provide clinical evidence of the cost effectiveness. But in the meantime, making the calculation and reporting of flow reserve as part of the examination might continue to provide evidence of the clinical value of nuclear cardiology.

The most virtuous attribute of molecular imaging is its contribution to understanding the mechanism of disease in a living organism. It is of paramount importance to identify appropriate targets, develop appropriate targeting probe, and develop appropriate radiolabeling technique. It is the only possible technique that can address subcellular mechanisms in vivo. Better understanding of pathogenetic mechanisms allows recognition of newer targets and hence yet better understanding.[21,22] Molecular imaging therefore would remain an important tool for imaging research for foreseeable future, even though the targeting probe and imaging methodology may evolve and change.

These are the best of times and the worst of times for molecular nuclear cardiology. To limit the impact of

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Dr. Carrio's Cassandra[1] like litany of the issues, we need to roll-up our sleeves and undertake the studies to apply our current procedures most effectively, validate the new procedures, and continue our quest for better understanding of the disease processes.

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[1] Webster New International Dictionary of the English Language, second edition, 1944. Cassandra was given the gift of prophecy by Apollo. Later, when Apollo became angry with her, he decreed that no one should believe her prophecies.